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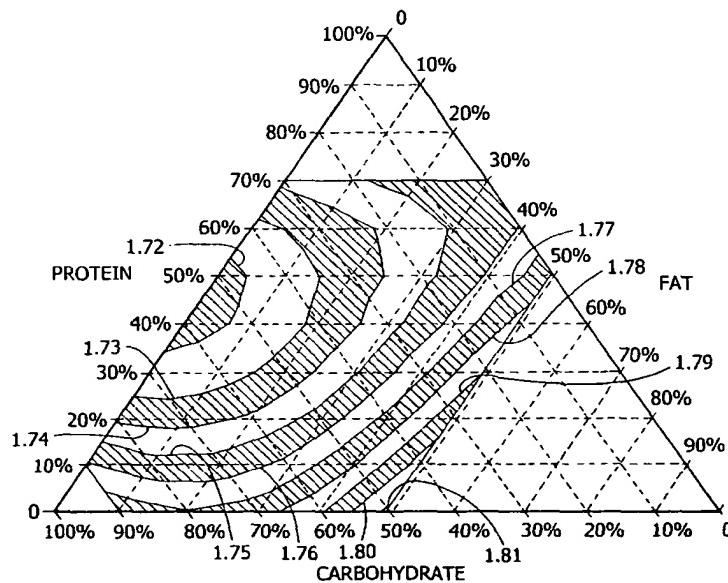
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- (54) Title: PARTICULAR FEED FOR YOUNG POULTRY



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- (57) Abstract: A particulate feed composition containing nutrients and moisture and a process for providing the particulate feed to poultry hatchlings during the first days of life to promote their health, growth, and disease resistance are disclosed. The particulate feed contains water, digestible carbohydrates, and amino acid sources and optionally other ingredients to provide nutrition, disease resistance, increase consumption, and/or enhance growth of the animals. The composition is a soft, moist, extruded particulate feed that is a size and consistency that is easily consumed by the hatchlings, resists release of water, and may be provided to the hatchlings by manual or automated means.



*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

**PARTICULATE FEED FOR YOUNG POULTRY**BACKGROUND OF THE INVENTIONField of the Invention

The present invention is directed to a particulate feed containing nutrients and moisture and a process for providing the particulate feed to poultry during the first days of life to promote their health, growth, and disease resistance.

Description of Related Art

10 The manner in which hatchling poultry are fed in the first few days of life makes a significant difference in their overall performance. A delay in their intake of feed and water can reduce early weight gains, negatively affect breast yield and other carcass characteristics, and slow 15 gastrointestinal and immune system development. Delayed early feeding directly contributes to mortality as well as to disease susceptibility in broiler chicks and other poultry hatchlings.

Poultry feeds have been formulated that contain high 20 concentrations of water to provide both nutrients as well as water to poultry. The feeds, such as those disclosed in WO 93/00017 (Forbes et al., 1993), can have a wet porridge or gruel consistency, and may be provided to poultry without also requiring water to be separately provided. Such feeds, 25 however, can release water in amounts that can dampen hatchlings or the floors of transportation containers upon contact or cause the food to stick to the hatchlings. Therefore, while water does not have to be separately provided, the risk of wetting hatchlings is still present.

30 In addition to the problem of wetting hatchlings, high moisture feeds often have handling and maintenance issues that are not well suited to the modern automated processes of the commercial poultry facilities. Such feeds typically require individualized handling in providing the feed to 35 hatchlings followed by cleaning of feed containers, pens, or transportation boxes. While permissible for small, non-

automated facilities, the additional handling and maintenance requirements increase costs and slow the processing of hatchlings in larger, automated facilities. In addition, the high moisture feeds also often have an 5 associated odor with the fresh feed as well as old, spilled feed as the feeds are comprised of a wet organic mixture.

Other high moisture feeds have also been formulated to provide gels or pastes that resist syneresis. These feeds may contain gelatinizing ingredients such as gelatin or 10 carrageenans. While these feeds may avoid the hazards associated with wetting hatchlings, the gel or paste feeds, like wet formulations, often require individualized handling in providing the feed to hatchlings followed by cleaning of feed containers, pens, or transportation boxes. The gels 15 and pastes typically do not flow easily with gravity to permit the feeds to be poured into hatchling boxes in an automated manner, but rather require individual handling to provide them to hatchlings. Furthermore, they may also have odors associated with both fresh feed and old feed that must 20 be cleaned out of feed containers and transportation boxes (Dibner, J., Feeding Hatchling Poultry: Avoid Any Delay, Feed International, Dec. 1999; Ivey, F. J. et al, U.S. Pat. No. 5,976,580; Friedman, H., U.S. Pat. No. 4,495,208; Lewis, D., U.S. Pat. No. 2,620,274;

25 The poultry gels and pastes also have a drawback of forming a leathery surface as moisture evaporates from the feed over time. A leathery surface may form rapidly in environments with elevated temperatures such as when the gels or pastes are placed in incubators for hatchlings to 30 eat immediately after hatching. When hatchlings eat, they will peck at dry food to either break large food particles into smaller consumable pieces. When the feed is in the form of a gel or paste, they will peck at and tear off small consumable pieces from larger gel or paste feed particles. 35 As the surface of gel or paste feeds becomes leathery over time, however, the hatchlings are unable to tear off and consume small pieces of the feed.

- Poultry gels and pastes have also been used in an extrudate form to facilitate their use in automated facilities. U.S. 5,976,580 discloses high moisture extrudates that are used as poultry feed. These high
- 5 moisture gels or pastes are pumped or compressed and forced through an opening directly to form an extrudate. This extrudate is provided in unit doses to locations where it may be eaten by hatchlings. The resulting extrudate therefore contains substantially the same amount of water as
- 10 the starting material. Thus, while the high moisture extrudates may reduce labor and be more suitable for automated poultry facilities, they also can become leathery and inedible by hatchlings as water evaporates from the surface of the extrudate.
- 15 It would therefore be beneficial to both large automated and smaller manual commercial poultry facilities to use a flowable poultry feed that provides both nutrients and water to hatchlings, resists syneresis, is a size that is easily consumable, remains consumable over time, and may
- 20 be provided in either manual or automated manners with low handling and maintenance requirements, and which has little to no associated odor.

#### SUMMARY OF THE INVENTION

Among the objects of the invention, therefore, is the

25 provision of a flowable feed which provides nutrients, water and other ingredients to promote the health, growth, and disease resistance to poultry or animals in the first days of their lives, the provision of a feed that remains soft, moist, that resists syneresis and which may be easily broken

30 up and consumed over time, the provision of a feed that is of an easily consumed size, the provision of a form of feed that can be provided to poultry or animals through automated processes, the provision of a feed that possesses little or no associated odor.

Briefly, therefore, the present invention is directed to a particulate feed for promoting the health, growth and disease resistance to poultry hatchlings. The particulate feed contains about 20% to about 35% water, at least about 5 30% by weight carbohydrates, and at least about 15% by weight of an amino acid source. The particulate feed, at the largest dimension of a particle, is preferably less than about 3.5 mm. The particulate feed may also contain a food coloring to promote consumption by poultry hatchlings.

10 The present invention is further directed to a process for promoting the growth, health, and disease resistance of poultry hatchlings. The process comprises feeding a particulate feed containing at least about 20% to about 35% water, at least about 30% by weight carbohydrates, and at 15 least about 15% by weight of an amino acid source. The particulate feed is fed to hatchlings within the first five days of hatching before the hatchlings are provided dry food ad libitum. The particulate feed, at the largest dimension of a particle, is preferably less than about 3.5 mm. The 20 particulate feed may also contain a food coloring to promote consumption by poultry hatchlings.

Other objects and features of the invention will be in part apparent and in part pointed out hereinafter.

#### BRIEF DESCRIPTION OF THE DRAWINGS

25 Fig. 1 is a bar graph illustrating the effect of fasting or feeding a particulate feed on intestine and yolk sack weight over 21 days in turkey hatchlings.

Fig. 2 is a bar graph illustrating the effect of fasting or feeding a particulate feed on bursa and spleen 30 growth over 21 days in turkey hatchlings.

Fig. 3 is a graph illustrating the appearance of biliary IgA in chicken hatchlings that were fasted or fed a particulate feed.

Fig. 4 is a bar graph illustrating the effect of the 35 particulate feed on resistance to coccidia in chicken hatchlings.

Fig. 5 is a graph illustrating the feed conversion efficiencies of mixtures containing protein, fat and carbohydrate.

DETAILED DESCRIPTION OF THE INVENTION

5 It has been discovered that the particulate feed of the present invention can stimulate the development of gastrointestinal and immune systems of poultry hatchlings. A hatchling's growth and weight gain are improved by stimulating early development of the gastrointestinal system. Similarly, the hatchling's health and hardiness throughout its life are improved by early development of its immune system. Furthermore, the feed conversion efficiency of the hatchling is ultimately improved by providing hatchlings with feed that meets their nutritional needs 10 during the early development and growth of their bodies. 15

The particulate feed preferably comprises relatively soft and moist particles of a size which is attractive to and may be readily consumed by hatchlings. In general, the feed particles preferably have a size (largest dimension) 20 which is no greater than about 4 mm, more preferably no greater than about 3.5 mm. Furthermore, the size distribution of particles is such that the largest dimension of the average particulate feed by weight is preferably between about 1.5 mm to about 3.5 mm; more preferably no 25 more than about 5% by weight of the particles have a size greater than about 3.5 mm, and no more than about 20% by weight have a size less than about 1.5 mm. Described in terms of mesh screen size, the particulate feed preferably has a size distribution such that at least 80% by weight of 30 the particulate feed is retained on a 12 mesh screen (1680 microns), less than 60% by weight is retained on an 8 mesh screen (2360 microns), and less than 5% by weight is retained on a 6 mesh screen (3350 microns). The preferred size of the particulate feed can be easily consumed by 35 hatchlings.

Preferably, the feed granules contain about 20% to about 35% by weight water to provide the desired degree of softness and moisture. In general, granules containing less than about 20% by weight water tend to be too dry and  
5 unattractive to hatchlings. On the other hand, granules containing more than about 35% by weight water can be difficult to prepare by the extrusion process of the present invention. Also, hatchlings may become weak or die if they are wetted (or dampened) by water released by the feed as a  
10 consequence of their brushing up against or otherwise coming into contact with it. Accordingly, it is generally preferred that the feed granules contain a moisture content near the upper end of this range when manufactured to allow for some moisture loss before the granules are offered or  
15 consumed by the hatchlings and, in addition, that the particulate feed avoid releasing water (syneresis) in an amount that could dampen a hatchling.

For ease of handling, the particulate feed preferably comprises free-flowing, relatively non-tacky granules that  
20 do not agglomerate under normal handling, such as when the particulate feed is poured or conveyed by hand or automated means into containers wherein the hatchlings are held. Preferably, the particulate feed has an angle of repose ranging between about 25° and about 60°, more preferably less  
25 than about 40°. Nevertheless, the particulate feed will typically possess some tack; for example, hand-compressing the particulate feed will preferably produce a loosely held together agglomerate of particulate feed, wherein individual particles of feed remain identifiable from each other such  
30 that the agglomerate can be broken up again into separate feed particles by hand. Applying greater force to the particle feed can cause the feed to agglomerate into a homogenous solid that subsequently is not easily broken up into feed particles. In addition to compression forces,  
35 the water content of the particulate feed also affects its tackiness and propensity to agglomerate. Thus, particulate feed containing about 35% by weight water will more readily

stick together under hand compression or even more readily form an homogenous solid under greater force than particulate feed containing about 20% by weight water.

The flowability of the particulate feed is superior over prior art high moisture extrudates in that it can be conveyed by gravity or mechanical means. While high moisture extrudates of the prior art (e.g. U.S. Pat. No. 5,976,580) are flowable by being provided to hatchlings in unit doses (i.e., by extruding a single, comparatively large mass into a container housing the hatchlings) through an extrusion opening, they flow only by being pumped or compressed and will not simply pour through the opening by gravity. Conversely, the size, shape, and lack of tackiness of the particulate feed permit it to be poured or flow freely by gravity.

The non-aqueous fraction of the particulate feed is sometimes referred to herein as the "dry matter." The dry matter fraction consists of digestible carbohydrates, an amino acid source, and optional ingredients, including fat, stabilizers, and food coloring agents. In addition, the particulate feed can be used as a delivery system to provide orally introduced bioactive substances such as vaccines, adjuvants, probiotics, vitamins, minerals, digestibility enhancers and the like to poultry hatchlings.

Carbohydrates provide a source of nutrition for the animals and, in addition, can aid in the formation of the solid feed. In general, digestible carbohydrates constitute at least about 18% by weight of the particulate feed, preferably at least about 30% by weight of particulate feed, more preferably about 35% to about 45% by weight of the particulate feed. The digestible carbohydrates contemplated herein include isolated carbohydrates such as corn starch, potato starch, wheat starch, rice starch, cellulose, pectin, agarose, and gums; bioavailable sugars such as glucose, fructose, and sucrose; chemically modified starches such as modified corn starch, methylcellulose, carboxymethyl-cellulose, and dextrin; humectants such as glycerol or

propylene glycol; corn syrup; invert sugar; and ground complex carbohydrates such as corn, rice, oats, barley, wheat, sorghum, rye, millet, cassava, triticale and tapioca, in whole, ground, cracked, milled, rolled, extruded,  
5 pelleted, defatted, dehydrated, solvent extracted or other processed form. Carbohydrates such as glucose may be chosen for high availability, or more complex sources such as ground corn or potato starch may be supplemented with enzymes or subjected to gelatinization to increase their  
10 availability. Preferable particulate feed carbohydrates include corn starch, corn syrup, and grain sources such as ground corn, rice, oats, barley, wheat, sorghum, rye.

To increase its nutritional value, the particulate feed preferably comprises at least about 15% by weight, more  
15 preferably about 15% to about 25% by weight of an amino acid source such as protein(s), amino acids, precursors or analogues of amino acids, and mixtures thereof. In addition, it is preferred that the weight ratio of all digestible carbohydrates to all amino acid sources in the  
20 particulate feed be between about 0.6:1 and 3:1, respectively. Exemplary amino acids are essential amino acids such as methionine, tryptophan, threonine, arginine and lysine. Exemplary amino acid precursors are 2-hydroxy-4-(methylthio)butanoic acid sold, for example, under the  
25 trademark Alimet® by Novus International (St. Louis, MO), and salts of 2-hydroxy-4-(methylthio)butanoic acid such as the calcium and sodium salts. Exemplary proteins include single cell proteins or hydrolysates of proteins such as those from yeast, algae or bacteria; isolated animal  
30 proteins, peptides or hydrolysates of proteins such as hemoglobin, myosin, plasma, or other serum proteins, collagen, casein, albumin or keratin; complex protein sources or hydrolysates of proteins such as milk, blood, whey, blood meal, meatmeal, feathermeal, fishmeal, meat and  
35 bone meal, poultry offal, poultry by-product meal, hatchery by-products, egg offal, egg white, egg yolk, and eggs without shells; plant protein or hydrolysate of proteins

such as soybean meal, soybean flour, isolated soybean protein, wheat protein, wheat germ, distillers grains and gluten. Preferable amino acid sources include vegetable protein sources such as soybean meal, isolated soybean 5 protein, soybean flour, corn gluten meal, and leguminous plant products, for example, peas, lupines, and rapeseed.

The digestibility of ingredients can be improved with additions to the formulation such as, but not limited to, enzymes, bile salts or surfactants. Similarly, overall 10 performance may be improved with the addition of selected micro ingredients, minerals, microorganisms, growth promotants, hormones, prostaglandins such as E<sub>2</sub> or other factors which promote enhanced digestive enzyme activity, nutrient absorption or maturation of the gastrointestinal 15 system as a whole.

In general, highly available protein sources might include hydrolyzed poultry protein, hydrolyzed casein, or peptone. In contrast, less available protein sources such as by-product meals or vegetable proteins might be fed in 20 combination with factors such as proteases or microorganisms that secrete proteases to increase digestibility.

Although not preferred for certain applications, fat may also be included in the particulate feed in relatively small proportions. A suitable particulate feed, therefore, 25 would comprise no more than about 5% by weight fat, preferably no more than about 2% by weight fat. Suitable fats include fatty acids such as linoleic acid; isolated plant oils such as sunflower, safflower, soybean, peanut, canola, corn, rapeseed, olive, linseed and palmkernal; fat 30 meals such as cottonseed, peanut, rapeseed, palmmeal and nut meals; and fats of animal origin such as egg yolk, lard, butter, poultry fat, tallow and fish oil.

To enable hatchlings to more effectively digest any fats which may be present in the particulate feed or to 35 enable the hatchlings to more effectively utilize its yolk-based lipid and protein, the particulate feed may contain bile salts, cholesterol, surfactants, emulsifying agents,

micelles, or an enzyme such as lipase, amylase, maltase, pepsin, trypsin, or other enzyme which commonly occur in the gastrointestinal system, or an enzyme such as keratinase which is not typically found in the gastrointestinal system 5 but which has useful activities. The concentration of the digestion aid will depend upon the application but, in general, will be between about 0.01% and about 5% by weight of the dry matter.

The particulate feed is preferably stabilized against 10 microbial growth, for example, by sterilizing, adding a microbial growth inhibitor such as methyl paraben or a sorbate to, or adjusting the pH of the mixture from which the particulate feed is formed. Preferably, the particulate feed is stabilized by adjusting the pH of the mixture with 15 an acid such as citric, propionic, phosphoric, sorbic, or fumaric acid to a pH within the range of about 3 to about 4, more preferably to a pH within the range of about 3 to 3.5. Such acid can be a low molecular weight carboxylic acid, preferably having a chain length of C<sub>2</sub> - C<sub>10</sub>, more preferably 20 having a chain length of C<sub>2</sub> - C<sub>7</sub>, most preferably having a chain length of C<sub>2</sub> - C<sub>5</sub>. Examples of useful carboxylic acids include citric acid, propionic acid, sorbic acid and fumaric acid. Citric acid, in addition to inhibiting microbial growth, serves as an energy source for the hatchlings. 25 Phosphoric acid can also be used.

The concentrations of the acids in the particulate feed vary by the acid selected and the pH of the non-acid ingredients. Citric acid and fumaric acid are preferably present in an amount of about 3.5% dry weight of the 30 particulate feed. Sorbic acid may also be included in an amount of preferably about 1.2% dry weight of the particulate feed. Phosphoric acid is preferably about 2.2% dry weight of the particulate feed.

Food coloring agents can be added to the particulate 35 feed as an attractant or to improve its visibility to hatchlings. The food coloring agents useful in the present invention include, for example, red, yellow, green, blue,

blue-green, black, and beige. Preferably, the food coloring agents of the particulate feed include red, blue, green, blue-green food coloring agents. More preferably, the food coloring agents of the particulate feed include blue, green,

5 blue-green food coloring agents, or a mixture thereof that results in a final particulate feed color that is preferably blue or green, more preferably a blue-green in color.

Examples of preferred color shades of the particulate feed include those falling within the color range from about

10 PANTONE MATCHING SYSTEM color reference PANTONE 305 CVC to about PANTONE 377 CVC, preferably PANTONE MATCHING SYSTEM color reference PANTONE 305 to 308 CVC, 311 to 315 CVC, 3115 CVC, 3125 CVC, 3135 CVC, 3145 CVC, 3155 CVC, 318 to 322 CVC, 325 to 329 CVC, 3252 CVC, 3262 CVC, 3272 CVC, 3282 CVC, 3292

15 CVC, 3255 CVC, 3265 CVC, 3275 CVC, 3285 CVC, 3295 CVC, 3258 CVC, 3268 CVC, 3278 CVC, 3288 CVC, 3298 CVC, 332 to 335 CVC, 338 to 342 CVC, 3385 CVC, 3395 CVC, 3405 CVC, 3415 CVC, 3425 CVC, 345 to 349 CVC, 352 to 356 CVC, 359 to 363 CVC, 366 TO 370 CVC, to about 373 to 377 CVC, more preferably

20 PANTONE MATCHING SYSTEM color reference PANTONE 325 to 329 CVC, 3252 CVC, 3262 CVC, 3272 CVC, 3282 CVC, 3292 CVC, 3255 CVC, 3265 CVC, 3275 CVC, 3285 CVC, 3295 CVC, 3258 CVC, 3268 CVC, 3278 CVC, 3288 CVC, 3298 CVC, 332 to 335 CVC, 338 to 342 CVC, 3385 CVC, 3395 CVC, 3405 CVC, 3415 CVC,

25 3425 CVC, 345 to 349 CVC, 352 to 356 CVC as viewed on PANTONE COLORWEB PRO, Version 1.0 (Pantone, Inc., Carlstadt, NJ).

The particulate feed may additionally be used as a vehicle to deliver a variety bioactive substances to poultry

30 and other animals. For example, the particulate feed may contain a peptide such as epidermal growth factor, transforming growth factor, granulocyte-macrophage colony stimulating factor, erythropoietin, bombesin, fibroblast growth factor, keratinocyte growth factor, nerve growth

35 factor, vascular endothelial growth factor, bovine or other somatotropin or insulin-like growth factor (IGF-I or IGF-II). The particulate feed may also contain a steroid or

polypeptide hormone such as, estrogen, glucocorticoids, insulin, glucagon, gastrin, calcitonin or somatotropin. The particulate feed may further contain an antibiotic approved for use in animal feed such as bacitracin, BMD (bacitracin 5 methylenedisalicylate), lincomycin, or virginiamycin or other therapeutic drug. The particulate feed may also additionally contain a natural or synthetic antioxidant such as ethoxyquin, tocopherol, BHT (butylated hydroxytoluene), BHA (butylated hydroxyanisole), vitamin C or glutathione; a 10 receptor, transfer factor, chelator or complexing agent which modifies release rates of nutrients or other bioactive compounds; an immunoactive agent such as cytokines, vaccines and other immunomodulators, immunoglobulins, antigens, killed cells, attenuated strains, toxins, or adjuvants.

15 These substances can be used alone or in combination with one another. The concentration of these additives will depend upon the application but, in general, will be between about 0.0001% and about 10% by weight of the dry matter, more preferably between about 0.001% and about 7.5%, most 20 preferably between about 0.01% and about 5%.

Vaccines useful in the present invention include those effective against common diseases in poultry such as Newcastle's Disease, Marek's Disease, infectious bursal disease, infectious bronchitis, enteritis, coccidiosis, etc. 25 These vaccines include Newcastle's vaccine, Marek's Disease vaccine, infectious bursal disease vaccine, infectious bronchitis vaccine, and Coccivac®, for example. When used in conjunction with the particulate feed of the present invention, these vaccines can be administered to young birds 30 within 0 to about 10 days of hatching orally, via yolk sac injection, subcutaneously, in ovo, or via inhalation by mist or spray.

Protozoal oocysts may also be added to the particulate feed to vaccinate hatchlings against coccidiosis. To 35 achieve desired immune system response against coccidiosis, live protozoal oocysts must be utilized. As oocysts would not survive the heat and pressure of the extrusion process,

live oocysts can be sprayed upon the surface of the particulate feed in concentrations that provide sub-clinical infections in hatchlings. Protozoa that may be utilized for coccidiosis vaccines include *Eimeria* spp. For example, 5 these can include *E. acervulina*, *E. maxima*, *E. tenella*, *E. mitis*, and *E. necatrix*, among others.

An adjuvant, that is, a substance that enhances the immune stimulating properties of an antigen to produce a non-specific stimulation of the immune system, may be 10 incorporated into the particulate feed. The preferred concentration of a selected adjuvant varies depending on factors such as the selected adjuvant, the degree of non-specific stimulation desired, the antigen, the selected vaccine used, and so forth. Exemplary adjuvants include 15 microbiologically-derived substances, viruses, lectins, polysaccharides, oils, peptides, polypeptides, and proteins, and various nucleic acids. Microbiologically-derived substances include materials produced by, or which are cellular components of, microorganisms such as bacteria, 20 fungi such as yeasts, etc. Such substances can be used as orally effective adjuvants in poultry to stimulate the immune system and/or to enhance the resistance of poultry to pathogens or other stresses, including exposure to heat or cold, dehydration, ammonia fumes in litter, transport, etc. 25 Thus, such adjuvants, when orally administered, can positively affect the health, livability, weight gain, or feed conversion efficiency of poultry.

Microbiologically-derived adjuvants comprise a variety of different types of substances. For example, these can 30 include lysates of bacteria such as *Haemophilus* sp., *Diplococcus* sp., *Neisseria* sp., etc.; trehalose 6,6-diesters (cord factor) and synthetic analogues thereof; muramyl dipeptide (*N*-acetyl-muramyl-L-alanyl-D-isoglutamine) and synthetic analogues thereof; L-seryl and L-valyl derivatives 35 of muramyl dipeptide; killed bacteria and derivatives thereof such as *Escherichia* spp, *Clostridia* spp, *Salmonella* spp, *Lactobacillus* spp, *Streptococcus* spp, *Bacillus*

Calmette-Guerin, *Mycobacterium* spp, *Bordetella* spp, *Klebsiella* spp, *Brucella* spp, *Propionibacterium* spp such as *Corynebacterium parvum*, *Propionibacterium acnes*, *Pasteurella* spp, *Nocardia* spp such as *Nocardia rubra* and derivatives thereof such as *Nocardia* water soluble mitogen; *Staphylococcus* cell wall products; bestatin; killed yeast such as *Saccharomyces* spp and *Candida* spp; yeast derivatives such as zymosan, glucan, and lantanin; endotoxins and enterotoxins such as *Cholera* toxin; cell wall peptido-glycans; and bacterial ribonucleoproteins. Microbiologically-derived adjuvants also include viruses, for example Avipoxviruses and Parapoxviruses.

Useful lectins include, for example, concanavalin A, pokeweed mitogen, and phytohemagglutinin.

Useful polysaccharides include mannans such as acemannan,  $\beta$ -(1,4)-linked acetylated mannan, and mannan oligosaccharide; glucans; carrageenan and iota carrageenan; hemicelluloses; levans; agar; tapioca; dextrans; dextrins, for example dextran sulfate salts of various molecular weights; and lipopolysaccharides.

Oil emulsions useful as adjuvants can be produced using mineral oil, peanut oil, and sesame oil, for example.

Useful peptides and macromolecules include cytokines such as lymphokines, interleukins, Transfer Factor, Macrophage Activating Factor, Migration Inhibitory Factor, and mitogenic factors for lymphocytes; nucleic acid digests; interferon and interferon inducers such as BRL 5907; double stranded complementary RNA homopolymers such as poly I:C and poly A:U; immune RNA; thymic hormones such as thymostimulin, thymulin, thymosin, and thymopoietin; protease inhibitors; chemotactic factors for macrophages and other cells; tuftsin; and serum albumin (bovine, human, acetylated derivatives, beads, etc.).

Finally, a variety of other substances that can be employed as adjuvants in the present invention include saponins such as QuilA and Iscoms; tiabenedezole; tylorone; statolon; maleic anhydride-divinyl ether; pyran copolymers;

amphotericin B; liposomes; silica; calcium phosphate; glycerol; betaine; protodyne; cyanidanol; imuthiol; picibanil; isoprinosine; lentinan; azimexon; lecithin; levamisole; vitamin A and other retinols; vitamin E and 5 other tocopherols; antioxidants, such as ethoxyquin; aluminum salts, such as sulfates and phosphates, including alum ( $KAl(SO_4)_2 \cdot 12H_2O$ ); aluminum hydroxide; and aluminum oxide.

Probiotics or direct fed microbials of bacterial, yeast 10 or mold preparations, can also be included in the particulate feed to provide various benefits such as altering the gastrointestinal microflora/microbiota of poultry and other animals. Those microbial additives which have been approved for use in animal feeds are identified in 15 the annual Feed Additive Compendium published by The Miller Publishing Company (Minnetonka, MN) in cooperation with The Animal Health Institute and the Direct-fed Microbial, Enzyme and Forage Additive Compendium published by The Miller Publishing Company. Among the direct-fed microbials which 20 have been approved are strains of the lactic acid bacteria, particularly those classified in the following genera: Lactobacillus, Lactococcus, and Enterococcus. Included among these are the following species: Lactobacillus reuteri, Lactobacillus acidophilus, Lactobacillus bulgaricus, Lactobacillus plantarum, Lactobacillus casei, Lactobacillus lactis, Lactococcus lactis, Lactococcus thermophilus, Lactococcus diacetylactis, and Enterococcus faecium. In addition to these lactic acid bacteria, some 25 species of Bacillus (such as Bacillus subtilis and Bacillus toyoji), some species of Streptococcus (such as Streptococcus faecium), and yeasts and molds (such as Saccharomyces cerevisiae, Aspergillus oryzae, and Torulopsis sp.) have 30 also been used as direct fed microbials. The amount of probiotics or direct fed microbials that may be added to 35 particulate feed is regulated by the Food and Drug Administration and identified in the annual Feed Additive

Compendium and the Direct-fed Microbial, Enzyme & Forage Additive Compendium.

The particulate feed of the present invention, therefore, may be used as a vehicle to administer direct-fed 5 microbials to poultry and other animals. When used for this purpose, the particulate feed should contain sufficient colony forming units of the yeast or bacterium to be of benefit to the animal. In general, the particulate feed used as a direct fed microbial should contain at least about 10 10<sup>2</sup>, preferably about 10<sup>4</sup>, and more preferably about 10<sup>6</sup> colony forming units of bacteria or at least about 10, preferably about 10<sup>2</sup>, and more preferably about 10<sup>4</sup> colony forming units of yeast per gram of composition. The yeast or bacterium may be incorporated into the particulate feed 15 prior to solidification or it may be deposited on or in the high moisture material after it has solidified. Although the particulate feed may be fed at anytime to alter the gastrointestinal microflora/microbiota of or provide other benefits to the animal, it is preferably fed to poultry as 20 soon as possible after hatching to establish the direct fed microorganism(s) as the dominant flora or culture in the gastrointestinal tract and thereby exclude potential pathogens.

The particulate feed may additionally contain vitamins 25 and minerals. Vitamin additives may be selected, for example, from vitamin A, B12, biotin, choline, folacin, niacin, pantothenic acid, pyridoxine, riboflavin, thiamin, C, D, 25-hydroxy D, E, and K. Mineral additives may be selected, for example, from calcium, phosphorous, selenium, 30 chlorine, magnesium, potassium, sodium, copper, iodine, iron, manganese and chromium pincolinate. The concentration of the vitamins and minerals will depend upon the application but, in general, will be between about 0.01% and about 5% by weight of the dry matter.

35 The amount of particulate feed that should be provided to hatchlings varies upon factors such as species, age, access to water, environmental temperature, and humidity the

length of time from hatch to shipment to grower facilities, the total transit time and the like should be considered when determining the amount of particulate feed to feed hatchlings. While the particulate feed is moist and 5 contains between about 20% to about 35% by weight water, it is typically still a much more dry food than either a gel, paste, porridge, or liquid food. As such, if it is provided in quantities of more than 10 grams per hatchling per day without also providing the hatchlings access to water, there 10 is a risk that the hatchlings will suffer from impacted crops. Generally, at least about 2 grams of high moisture material per chick per day should be provided to 0 to 2 day old chicks, about 4 to 5 grams of high moisture material per chick per day should be provided to 2 to 3 day old chicks, 15 and up to about 8 to 9 grams of high moisture material per chick per day should be provided to 4 to 7 day old chicks. Greater quantities of feed may be given to hatchlings provided they have access to water.

In one extrusion process, dry ingredients, for example, 20 ground corn, soybean flour, anhydrous citric acid, and sorbic acid, are mixed together to form a dry mixture. During the mixing process, the dry ingredients may be subjected to grinders or other equipment that can grind or break down larger raw materials into smaller sizes.

25 The dry mixture is combined in an extruder with water and other ingredients, for example, corn syrup, phosphoric acid, propionic acid, food coloring, or other ingredients described herein. The ingredients are added in amounts to preferably produce a particulate that contains about 20% to 30 about 35% water. The extruder mixes and heats the combined ingredients to form a feed mixture. The feed mixture is pumped under pressure through an orifice or extrusion die of a desired dimension to produce an extrudate. The width of the orifice or extrusion die determines the diameter of the 35 particulate feed. The orifice or extrusion die width is preferably 2.0 mm to 3.0 mm wide, more preferably 2.0 mm to 2.5 mm wide. A 2.0 mm to 2.5 mm die is more preferred as it

produces a size of particulate feed that hatchlings can easily peck at, break up, and consume. As the size of extrudate increases, the hatchlings have increasing difficulty in breaking up and eating the extrudate.

5       As the feed mixture emerges from the orifice or extrusion die, a cutter or knife cuts the emerging feed mixture into desired lengths. The cut lengths of extrudate are subsequently cooled to produce a flowable feed that preferably have a size (largest dimension) which is no  
10 greater than about 4 mm, more preferably no greater than about 3.5 mm. The size distribution of the flowable feed is such that the largest dimension of the average particulate feed by weight is preferably between about 1.5 mm to about 3.5 mm; more preferably no more than about 5% by weight of  
15 the particles have a size greater than about 3.5 mm, and no more than about 20% by weight have a size less than about 1.5 mm.

After cooling from the extrusion process, the particulate feed is a free-flowing granulation with an angle of repose preferably ranging between about 25° and about 60°, more preferably less than about 40°. The particulate feed can therefore be provided to hatchlings through manual or automated means by pouring the particulate into hatchling containers within its free-flowing angle of  
25 repose.

Newly hatched birds typically spend a period of time in the hatchery and in transport before they are placed in a poultry grower facility. If no outside source of nutrition is available during this period, the hatchlings must rely  
30 upon nutrients present in their yolk sacs. The present invention provides a particulate feed and method of feeding that provides hatchlings both nutrients and water needed in their first days after hatching.

The industry practice in hatcheries is to ship  
35 hatchlings to poultry grower facilities within about two days of hatching. This practice has developed, in part, out of the fact that hatcheries typically do not provide food or

water to the hatchlings and the fact that the hatchlings will suffer if they do not receive water and a source of nutrition by about three days after hatch. Since particulate feed can provide both initial food and moisture to hatchlings, hatcheries may be able to delay sending hatchlings to poultry grower facilities for a longer period of time. Additionally, hatchlings may be shipped a greater distance without experiencing many of the difficulties associated with providing water and nutrition to the hatchlings.

The particulate feed provides both poultry hatcheries and poultry grower facilities greater flexibility during the initial days of the hatchlings' lives. As the hatchlings can immediately begin consuming the particulate feed after hatching, the hatcheries are not be under time pressure to have the hatchlings arrive at the poultry grower facility by the third day. Instead of fasting the hatchlings and shipping them within two days of hatch, hatcheries can provide them with the particulate feed for several days from hatching while additional poultry are hatched. Thus, the hatcheries can make fewer shipments of greater quantities of hatchlings. This allows hatcheries flexibility in their shipping schedules without risking the health of the hatchlings or requiring the hatcheries to expend additional resources to both feed the hatchlings dry food and provide water.

Early feeding has a greater effect than simply giving hatchlings a "head start" over those for which feeding is delayed for a day or two. The particulate feed, when consumed in the first days following hatching, can help achieve optimum gut development and immune competence which have positive long term effects throughout the hatchling's life. Early feeding can also improve hatchlings' response to vaccinations and is associated with increased disease resistance later in life. Therefore, initially feeding the particulate feed to hatchlings from the time they hatch until they are offered dry food or allowed to drink water ad

libitum results in improvements in their health, growth, and disease resistance by stimulating the development of their gastrointestinal and immune systems.

In one embodiment, the particulate feed is a soft, moist bead or granule that is manufactured through an extrusion process. The particulate feed, when initially offered to hatchlings, should contain at least about 20% by weight water (an amount which is in excess of the amount of water contained in "dry" poultry feeds), and preferably between about 20% and about 35% by weight water, based upon the weight of the particulate feed. The moisture content of the particulate feed provides adequate supply of water in the first day of life. Hatchlings can absorb the balance of water they need to survive from the residual yolk, which contains about three grams of water at the time of hatch.

When hatchlings are transported from the hatchery to a poultry grower facility, they are typically placed in boxes in capacity numbers. This causes the hatchlings to brush against each other, the floor and sides of the box, and any food or other objects placed in the transportation boxes. If either a hatchling or the interior of the box becomes wet or damp, the confined space of the transportation box can cause other hatchlings to become damp as they either brush against the box or each other. It is therefore necessary that any food provided in the chick boxes does not release sufficient amounts of water to result in dampening the hatchlings or the floor or sides of the box.

The particulate feed provides hatchlings with a significant amount of dietary moisture to supplement their water needs without releasing sufficient water to wet or dampen the hatchlings or transportation container floors or walls. Additionally, the particulate feed is produced in an extrusion process that incorporates water and humectants into a mixture of dry ingredients thereby permitting it to maintain soft and moist over time. Particulate feed that is soft and moist permits the hatchlings to peck at, break up, and consume the feed without requiring water to be

simultaneously provided. Furthermore, the particulate feed will not form a tough, leathery skin that prevents hatchlings from tearing off or breaking the feed into consumable pieces. The ability of the particulate feed to 5 maintain its moisture content is significant as poultry hatchlings typically will not consume dry feed (i.e. feed containing less than 20% water) without being provided water to drink.

In another embodiment of the present invention, the 10 particulate feed is first fed to poultry hatchlings which are within five days of hatching. Preferably, the particulate feed is fed to the hatchlings before they are offered dry food or allowed to drink water ad libitum, and more preferably, before they are offered dry food at all. 15 For example, the particulate feed may be placed in the incubator boxes containing the eggs from which the poultry will hatch so that the particulate feed is available to the hatchlings immediately upon hatching. Providing the particulate feed to the hatchlings prior to their 20 introduction to dry feed provides the hatchlings with nutrients and water in their initial stages of life.

In another embodiment of the present invention, the particulate feed may be made available to the hatchlings prior to or during their shipment to poultry grower 25 facilities. In this embodiment, the particulate feed is placed with the hatchlings in the transportation boxes so that the hatchlings will have the opportunity to consume the particulate feed while they are shipped to poultry grower facilities. This permits hatchlings to begin feeding during 30 transit to poultry grower facilities, thereby providing them with oral nutrients and moisture needed to develop and maintain biomolecules present in their yolk sacs available for passive immunity purposes.

In a further embodiment of the present invention, the 35 particulate feed alone, with or without water, is fed to the poultry after they arrive at either a poultry grower facility or an intermediate facility until they begin eating

dry food and drinking water ad libitum. Hatchlings often do not immediately transition to eating dry food, thus the particulate feed may be provided to the hatchlings as feed until they make the transition.

- 5        In still another embodiment, the particulate feed can be used to promote transitioning the hatchlings to dry feed by sprinkling the particulate feed over the top of dry feed (top dressing the feed). The hatchlings, having been previously introduced to the particulate feed in the  
10      incubator, in transportation boxes, and/or as a sole feed source, are attracted to the particulate feed as food. If the particulate feed is sprinkled on top of dry food, the hatchlings will begin pecking and consuming the particulate feed and dry feed. Thus, the hatchlings will transition to  
15      consuming dry feed ad libitum.

The particulate feed may also be utilized to administer drugs or other substances to poultry as described herein.

The following examples will illustrate the invention.

#### Example 1

- 20       The effect that early nutrition has on gut weight and yolk sac weight as a percent of total body weight was studied in which turkey hatchlings fed the particulate feed during days 0 to 4 after hatching were compared to turkey hatchlings that were fasted during the same time period.  
25       The results of the study are outlined in Fig. 1.

The development of the hatchlings' small intestines, which is necessary for normal development in the hatchlings, is evidenced by increased intestine weights. In terms of body weight, the fasted hatchlings lost an average of  
30      1.12 grams, while hatchlings that were fed the particulate feed gained an average of 1.0 grams over the four day treatment.

As evidenced by the results of Fig. 1, oral intake of food is required for growth and development of the  
35      hatchlings' gastrointestinal system. While potential nutrients are present in the yolk sac for all birds, the

increase in gut weight does not occur if the residual yolk is used for nutrition. Thus, as observed in Fig. 1, the small intestine growth was significantly greater in the fed birds.

- 5 While hatchlings are able to utilize their yolk sacs, the rate of utilization of the yolk sac was not changed by fasting. Relative yolk sac weight (*i.e.* yolk sac as a proportion of body weight), was greater in fasted birds, which in part was the result of a decrease in body weight.
- 10 Absolute yolk sac weights, however, did not indicate an acceleration of utilization of the yolk in fasted birds.

Example 2

A study was conducted to identify the effect of early feeding of particulate feed on the bursa and spleen of 15 hatchlings. The bursa and spleen are primary and secondary immune system organs in birds. The bursa and spleen each produce lymphocytes, or white blood cells, that are active in immune responses to antigens. The study consisted of feeding the particulate feed to turkey hatchlings during 20 days 0 to 4 after hatching. A second group of turkey hatchlings was fasted during the same period. The study continued for a period of 21 days after which the bursas and spleens of the two groups were compared.

The results, which are outlined in Fig. 2 indicate that 25 the bursa and spleen of hatchlings that were fed the particulate feed were heavier than those of the fasted group. Conversely, the lack of nutrients, hormone responses to fasting, or oral antigen deprivation during the first days of a hatchling's life appear to affect the bursa and 30 spleen weight on a long term basis. Thus, initially feeding hatchlings particulate feed during the first days of their life could improve their resistance to disease while fasting hatchlings may have the opposite effect.

Example 3

A study of biliary IgA levels broiler chicks suggests that the practice depriving hatchlings of food and water in their initial days of life may cause long-term negative consequences to key immune functions. Biliary IgA is an immunoglobulin that is a part of the mucosal immune system and critical for disease resistance in the gastrointestinal and respiratory systems. The study consisted of feeding the particulate feed to broiler chicks during days 0 to 4 after hatching. A second group of broiler chicks was fasted during the same period. The study continued for a period of 21 days during which the IgA levels of the two groups were measured and compared. The results of the study on biliary IgA on broiler chicks is outlined in Fig. 3.

As indicated in Fig. 3, hatchlings that were initially fed the particulate feed in their first days of life had significant levels of biliary IgA earlier than fasted hatchlings. In addition, the day by day levels of IgA which were measured from day 8 through the end of the study were greater in the group that was fed the particulate feed than the IgA levels measured in the fasted group.

Example 4

The negative effects of fasting on hatchling's immune systems may directly affect the bird's response to a vaccine and their overall resistance to disease. Research was conducted on two groups of turkey hatchlings. The first group of hatchlings (treatments 1, 3, 5, and 7) were fed nothing for the first 2 days of life while the second group (2, 4, 6, and 8) was fed the particulate feed for the same period. Additionally, the hatchlings of treatments 5 to 8 were immunized on days 0 and 1 using a commercial coccidiosis vaccine (Coccivac-B, American Scientific Laboratories, Inc., subsidiary of Schering-Plough Animal Health, Union, N.J.) at the recommended dosage. Hatchlings in treatments 2, 4, 7 and 8 were challenged on day 14 using

a high dose (100 doses per 100 grams body weight) of the coccidiosis vaccine.

The results, as summarized in Fig. 4, show that the hatchlings that were fed the particulate feed had significantly greater body weights on day 20 in all treatments when compared to the fasted controls. Feeding the hatchlings the particulate feed not only resulted in superior performances of the vaccinated, challenged hatchlings (treatment 8) to resist the disease challenge, but also resulted in improved resistance of the non-vaccinated hatchlings (treatment 4) when compared to the fasted controls (treatments 3 and 7).

The data indicate that feeding hatchlings the particulate feed in the first days of their lives improves the general performance of the hatchlings and their ability to respond to a disease challenge, whether vaccinated or not over fasted hatchlings. Furthermore, the data suggest that hatchlings receiving an optimum nutrient formulation immediately after hatch are better able to respond to physiological and environmental challenges present in the poultry industry.

The above Examples illustrate that the particulate feed improved the general performance of poultry hatchlings and their ability to respond to a disease challenge when fed to the hatchlings immediately after hatch. Furthermore, the beneficial effects of initially feeding particulate feed to hatchlings was seen later in their lives, long after the feeding of the particulate feed ended and the hatchlings began to eat dry food and drink water ad libitum.

30 Example 5

An experiment was conducted to determine the optimum ratio of fat, protein, and carbohydrate in a poultry feed formulation. An experimental design was generated to meet the stated objective and it was implemented as a 96 pen, 35 41 day study. In this study, 1-4 day old chicken hatchlings were fed the formulation or were fasted for 48 hours. The

results are present in Figure 5. The performance parameter illustrated in Figure 5 is the estimated feed conversion for a 2kg broiler at 41 days. The percentages given in Fig. 5 represent the percentages of fat, protein, and carbohydrate 5 in the dry matter portion of the total formulation. A response surface model was made for feed conversion corrected to a constant live weight. It was found that fat had a large negative impact on performance. The birds treated with greater than 20% fat in the total dry matter 10 showed losses in live weight and increased feed conversion. The best performance occurred with the protein and carbohydrate treatments where the birds exhibited body weight corrected feed conversions of 1.72-1.73. This occurred when protein was between 20% to 70% of the total 15 dry matter and carbohydrate was between 30% to 80% of the total dry matter. Mortality was lowest at 21 days for treatments with higher levels of protein, and highest with treatments that contained significant amounts of fat.

In view of the above, it will be seen that the several 20 objects of the invention are achieved.

As various changes could be made in the above compositions and processes without departing from the scope of the invention, it is intended that all matter contained in the above description be interpreted as illustrative and 25 not in a limiting sense.

WHAT IS CLAIMED IS:

1. A particulate feed for enhancing the health livability, cumulative weight gain or feed conversion efficiency of poultry hatchlings comprising about 20% to about 35% by weight water, at least 18% by weight digestible carbohydrates, and at least about 15% by weight of an amino acid source, wherein the size distribution of particles is such that the largest dimension of the average particulate feed by weight is between about 1.5 mm to about 3.5 mm.  
5
2. The particulate feed of claim 1 wherein the largest dimension of the particulate feed is less than about 3.5 mm.
3. The particulate feed of claim 1 wherein no more than about 5% by weight of the particles have a size greater than about 3.5 mm, and no more than about 20% by weight have a size less than about 1.5 mm.
4. The particulate feed of claim 1 further comprising a food coloring agent.
5. The particulate feed of claim 1 wherein the particulate feed has a color selected from the group consisting of blue, green, or blue-green.
6. The particulate feed of claim 1 wherein no more than about 5% by weight of the particles have a size greater than about 3.5 mm at the largest dimension of the particle and no more than about 20% by weight have a size less than about 1.5 mm at the largest dimension of the particle.  
5
7. A particulate feed for enhancing the health livability, cumulative weight gain or feed conversion efficiency of poultry hatchling comprising about 20% to about 35% by weight water, about 35% to about 45% by weight digestible carbohydrates, about 15% to about 25% by weight

of an amino acid source, and no more than about 5% by weight fat, wherein the size distribution of particles is such that the largest dimension of the average particulate feed by weight is between about 1.5 mm to about 3.5 mm.

8. The particulate feed of claim 7 wherein no more than about 5% by weight of the particles have a size greater than about 3.5 mm, and no more than about 20% by weight have a size less than about 1.5 mm.

9. The particulate feed of claim 8 containing a food coloring agent is a color selected from the group consisting of red, blue, green, or blue-green.

10. The particulate feed of claim 8 wherein the particulate feed has a color selected from the group consisting of blue, green, or blue-green.

11. The particulate feed of claim 10 further comprising one or more ingredients selected from the group consisting of acid stabilizers, vaccines, adjuvants, probiotics, vitamins, and minerals.

12. A process for enhancing the health, livability, weight gain or feed conversion efficiency of poultry, the process comprising feeding a particulate feed containing about 20% to 35% by weight water, at least 35% by weight digestible carbohydrates, and at least about 15% by weight of an amino acid source to the poultry before the poultry is offered dry food ad libitum, wherein the largest dimension of the particles is less than about 4 mm.

13. The process of claim 12 further comprising a food coloring agent.

14. The process of claim 13 wherein the food coloring agent is a color selected from the group consisting of red, blue, green, or blue-green.

15. The process of claim 12 wherein the particulate feed is placed in close proximity to dry feed.

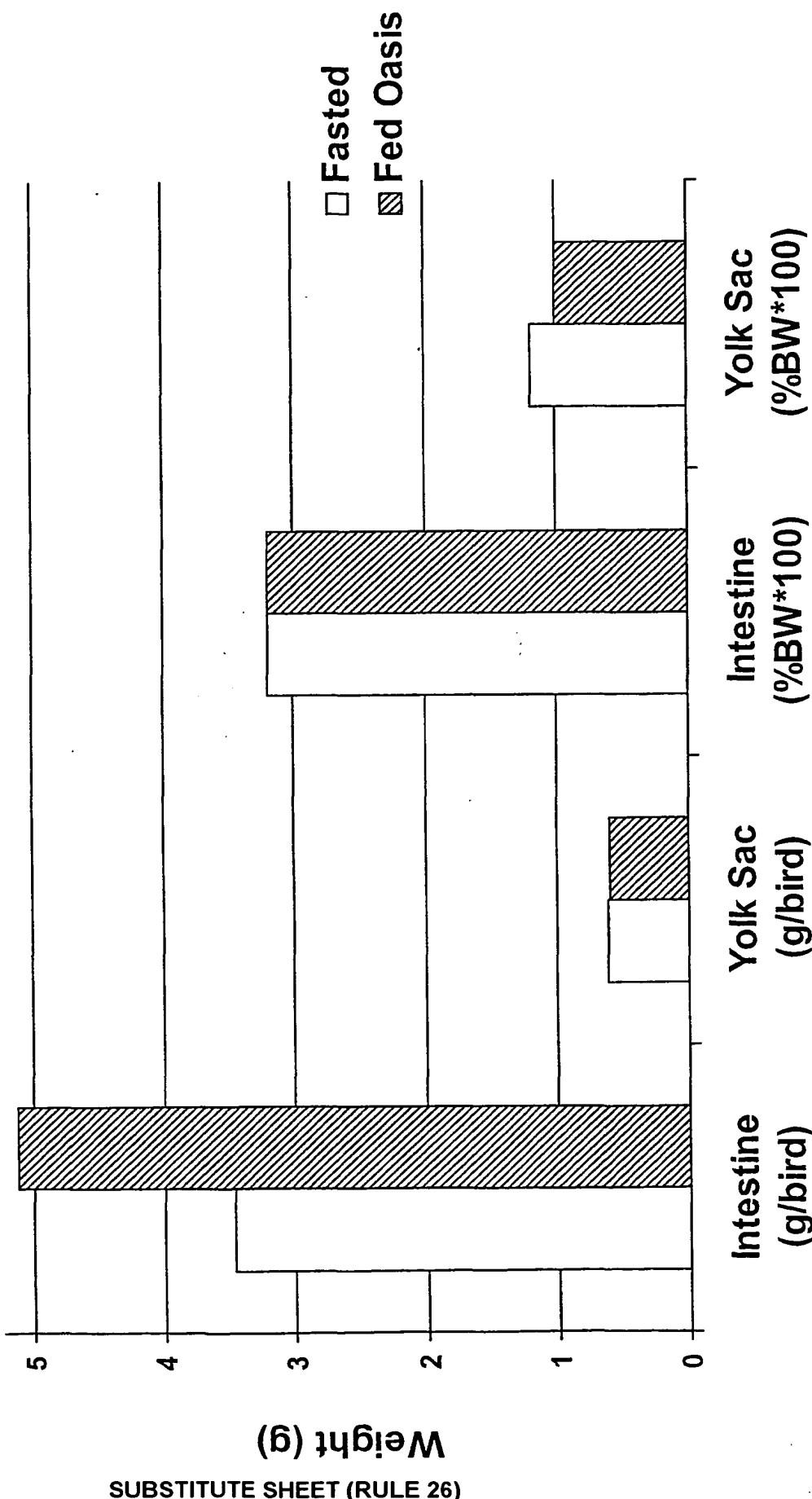
16. The process of claim 12 wherein the largest dimension of the particulate feed is less than about 3.5 mm.

17. The process of claim 12 wherein the largest average dimension of the particulate feed by weight is between about 1.5 mm to about 3.5 mm.

18. The process of claim 12 wherein the particulate feed further comprises one or more ingredients selected from the group consisting of acid stabilizers, vaccines, adjuvants, probiotics, vitamins, and minerals.

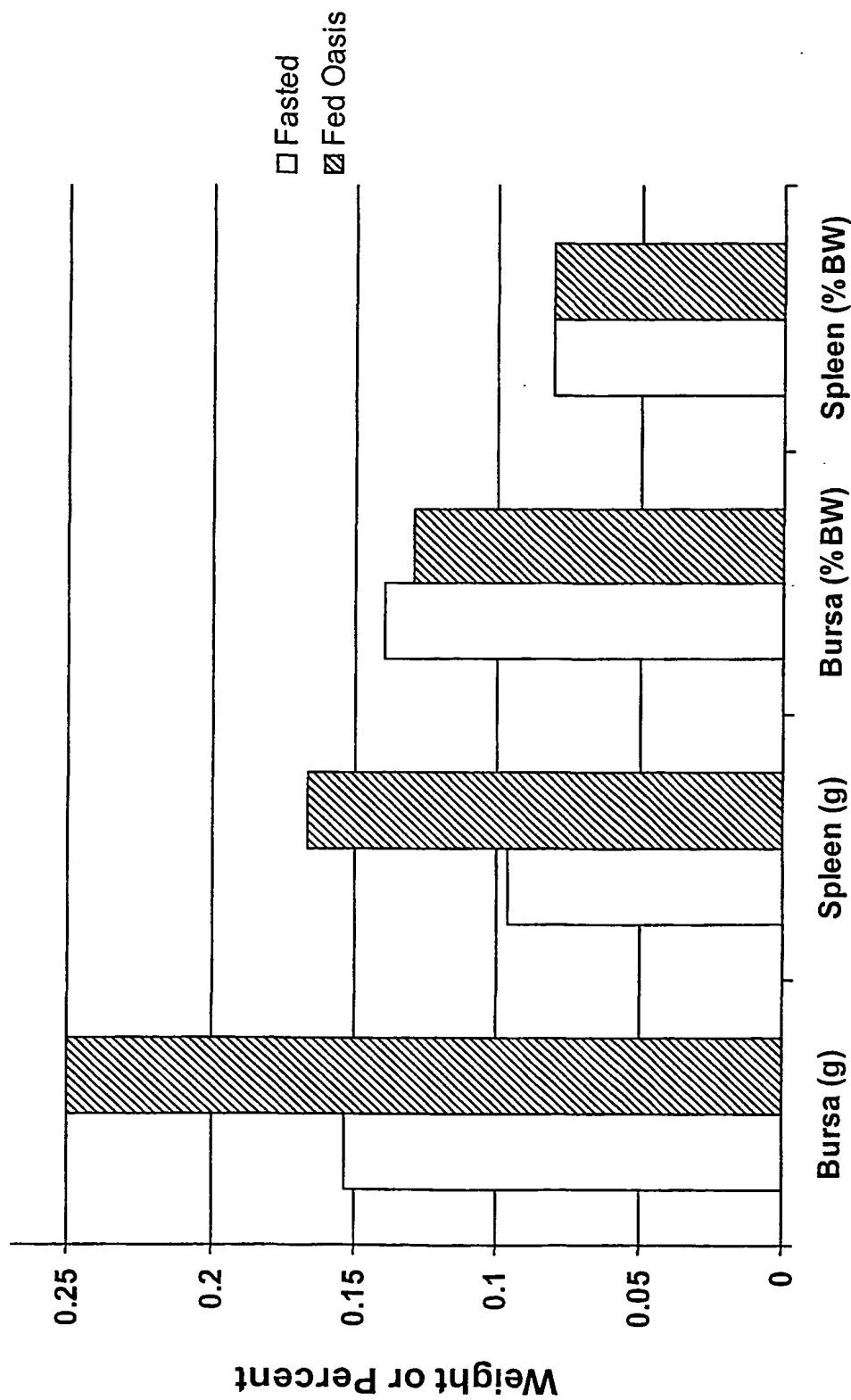
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**FIG. 1 Effect of Fasting or Feeding Oasis® on Intestine and Yolk Sac Development**



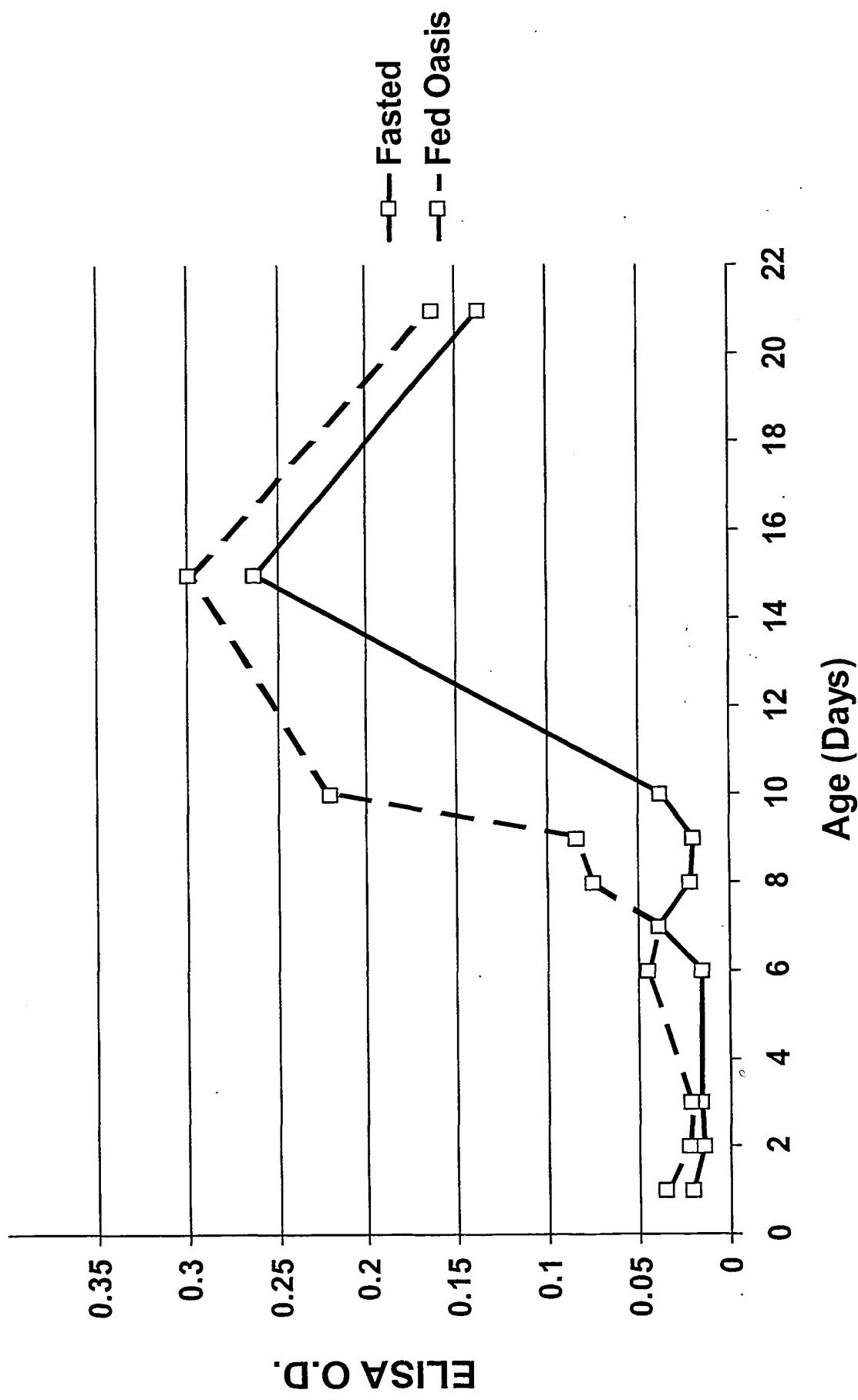
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**FIG. 2****Effect of Fasting or Feeding Oasis (Days 0-4)  
on Growth of Bursa and Spleen in Poults over 21 Days****SUBSTITUTE SHEET (RULE 26)**

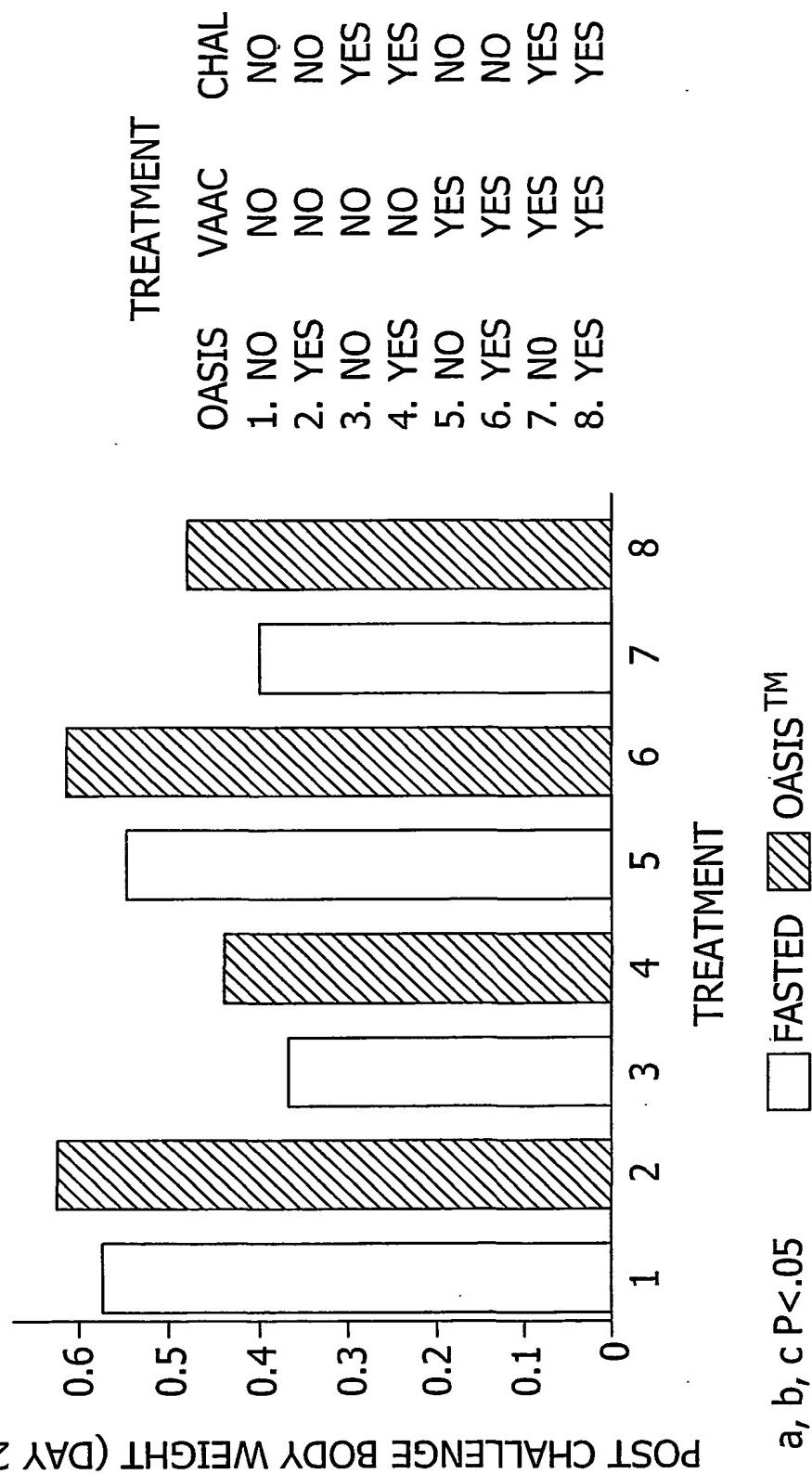
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**FIG. 3**  
**Effect of Early Feeding on Biliary IgA**



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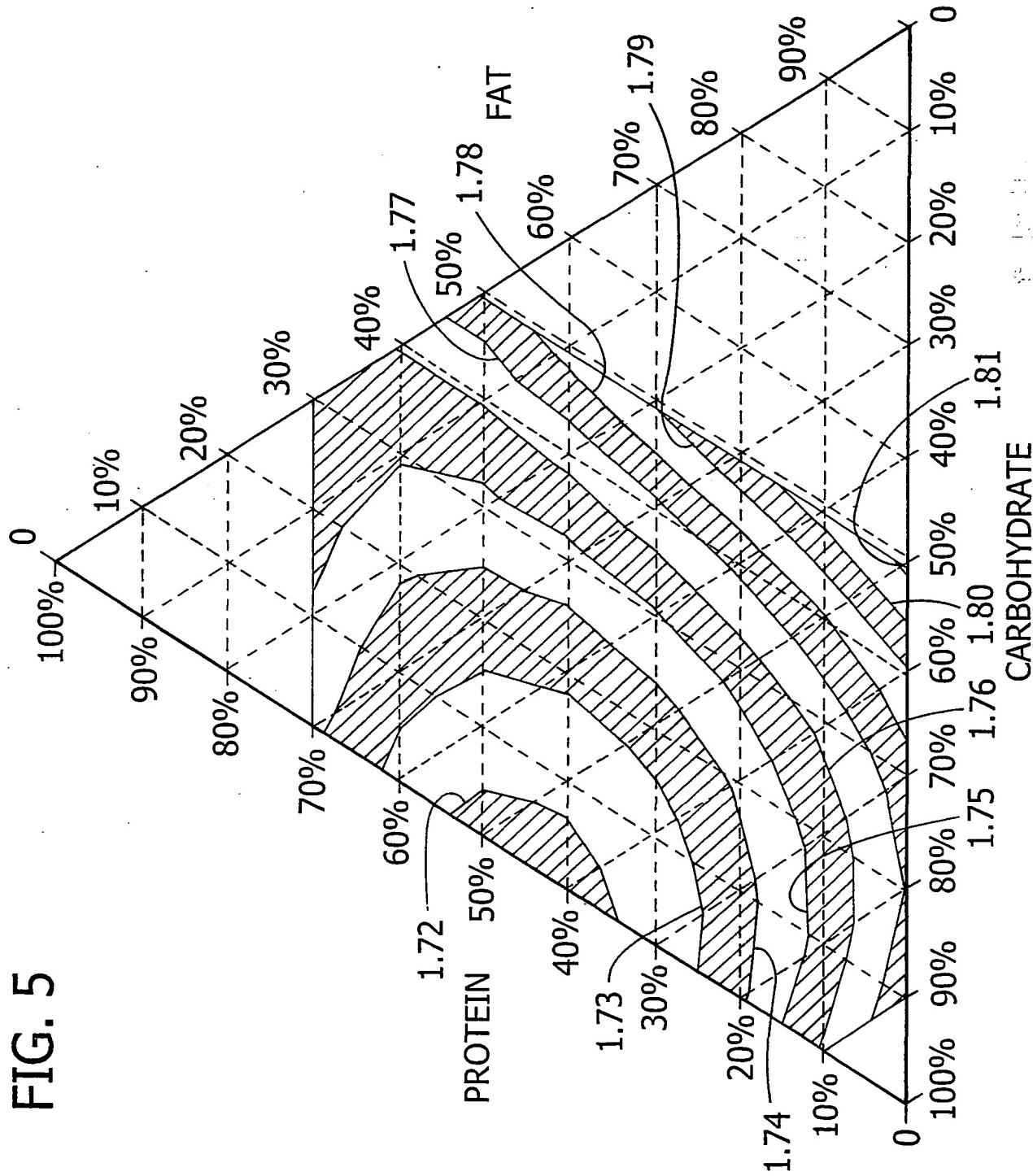
FIG. 4



EFFECT OF A HATCHLING SUPPLEMENT ON RESISTANCE TO COCCIDA IN BROILERS

5/5

FIG. 5



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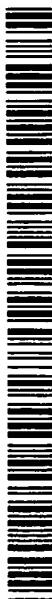
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**WO 01/91574 A3**

(54) Title: PARTICULATE FEED FOR YOUNG POULTRY

(57) Abstract: A particulate feed composition containing nutrients and moisture and a process for providing the particulate feed to poultry hatchlings during the first days of life to promote their health, growth, and disease resistance are disclosed. The particulate feed contains water, digestible carbohydrates, and amino acid sources and optionally other ingredients to provide nutrition, disease resistance, increase consumption, and/or enhance growth of the animals. The composition is a soft, moist, extruded particulate feed that is a size and consistency that is easily consumed by the hatchlings, resists release of water, and may be provided to the hatchlings by manual or automated means.

# INTERNATIONAL SEARCH REPORT

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PCT/US 01/14937

**A. CLASSIFICATION OF SUBJECT MATTER**  
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According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 A23K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CAB Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GB 2 102 268 A (NIPPON FORMULA FEED MFG) 2 February 1983 (1983-02-02) page 1, line 33 - line 53 page 1, line 62 -page 3, line 2 page 2, line 30 - line 34 examples 1,2 claim 1 ---	1,7,12
Y	US 5 976 580 A (DIBNER JULIA J ET AL) 2 November 1999 (1999-11-02) cited in the application column 6, line 29 - line 62 claims 1,38,39 ---	1,7,12

Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/14937

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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